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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,508	08/01/2001	Tatsuo Kakimoto	Q65478	3296

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SUGHRUE, MION, ZINN,
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EXAMINER	
KAPUST, RACHEL B	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,508	KAKIMOTO ET AL.	
	Examin r	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication app ars on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *9-19 and 22-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,20 and 21* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6,7*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, directed to methods for analyzing agonist-activity to a cytokinin receptor, is acknowledged. The traversal is on the ground(s) that Applicants argue that Groups I and V should be rejoined because the groups share the same subclasses and undue burden in searching would not be required. Applicant's arguments are found to be persuasive, and Groups I and V are rejoined.

Claims 9-19 and 22-27 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.48(b).

Claims 1-8 and 20-21 are under consideration.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on pages 12 and 22. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The use of the trademarks Takara Heraculase™, Takara LA taq™, Phytagel™, Oligotex™, and FPLC pure™ have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 8 is objected to because of the following informalities: in the last line of claim 8, cytokinin is misspelled as "cyctokinin". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, 8, 20, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite in the recitation of "a cell having a function of" directly controlling cell growth by intracellular signal transduction. It is the cytokinin receptor that has this function, not the cell.

Claim 3 is indefinite because, as written, the cell has a lower histidine kinase activity than itself.

Claim 4 is indefinite because, as written, the cell has a lower histidine kinase activity than its intrinsic activity and thus, as in claim 3, has a lower histidine kinase activity than itself. Further, "intrinsic" is itself indefinite; such activity would not be static and the skilled artisan would not be able to determine what level as "intrinsic".

Claim 8 is indefinite in the recitation of "natural form" in (d) since forms of different structure could also occur in nature and the skilled artisan would be unable to determine what forms the claim was intended to encompass.

Claims 20 and 21 are indefinite in the recitation of "section"; the origin of "section" is not specified. These claims are also indefinite in the recitation of "based on the difference obtained by comparison". The skilled artisan would not be able to determine what parameter Applicant intended to evaluate.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for analyzing agonist-activity to a cytokinin receptor wherein the cytokinin receptor comprises SEQ ID NO: 2, 4 or 6, does not reasonably provide enablement for a method for analyzing agonist-activity to any cytokinin receptor or a cytokinin receptor wherein the receptor comprises SEQ ID NO: 2, 4, or 6 and has deletions, substitutions, or additions of a plurality of amino acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention; 2) state of the prior art; 3) relative skill of those in the art; 4) level of predictability in the art; 5) existence of working examples; 6) breadth of claims; 7) amount of direction or guidance by the inventor; and 8) quantity of experimentation needed to make and/or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Applicants state that a cytokinin receptor is a "protein having functions of controlling the propagation and differentiation of cells of higher plants" (p. 10). However, while it is known that cytokinins promote the growth of lateral buds, stimulate chloroplast development, and delay senescence in leaves, almost nothing is known about how cytokinins function at the cellular level (Estelle (1998), *Current Biology* 8: R539-R541). Two signaling pathways have been characterized: a G-protein-coupled receptor pathway, and a two-component histidine kinase pathway (Estelle, p. R539, column 1), but not much is known about the pathways. It is not known whether some cells use only one signaling pathway or if the pathways function in the same cell. Moreover, it is not known how the separate pathways interact. Thus, because of the diversity amongst the cytokinin receptors and the fact that signaling pathways of cytokinin receptors still need to be elucidated, the statement that a protein is a cytokinin receptor provides no guidance as to its actual biological function or activity. One of skill in the art would not be

able to make DNA encoding a cytokinin receptor, and one of skill in the art would therefore not be able to analyze agonist activity to cytokinin receptors.

Applicants define "a plurality of amino acids" as about 2 to 20 amino acids (p. 10-11). Applicants further state that when one or a plurality of amino acids is deleted, substituted, or added, the overall amino acid sequence will be at least 80% identical with the amino acid sequence before the deletion, substitution, or addition occurred (p. 11). Applicants have not provided any examples of amino acid substitutions, additions or deletions that would lead to cytokinin receptors that control propagation and differentiation of cells of higher plants. The amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be deleted or inserted or substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure and function from mere sequence data are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, whereas other positions may be substituted or deleted without affecting the protein's structure/function relationship. A person of skill in the art would not know whether a cytokinin receptor variant controls propagation and differentiation of cells until the gene is cloned, the protein is expressed, and growth assays are performed.

Since detailed information regarding the structural requirements of the cytokinin receptor variants is lacking, the state of the prior art, the unpredictability of the art, the lack of working examples, the breadth of the claims, and the lack of direction provided by the Applicants, it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

Claims 1, 3-8, 20, and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of analyzing agonist activity by measuring the quantity of cell growth of a transformed cell, does not reasonably provide enablement for methods of analyzing agonist activity by measuring the existence or quantity of any intracellular signal transduction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As stated above, almost nothing is known about how cytokinins function at the cellular level (Estelle, p. R539, column 1). In fact, much of what is known about two-component systems arises from studies in bacteria, and it is not clear what the differences are between the signaling pathways in plants and bacteria (Schaller (1997), *Essays Biochem.* 32: 101-11, p. 102). It appears that the only known responses of cytokinin receptors to cytokinins are the induction of cell division, chloroplast development, formation of shoots/buds, and delayed senescence in leaves. Thus, one of skill in the art would not know what other responses to look for when analyzing agonist activity.

Because of the state of the prior art, the unpredictability of the art, the lack of working examples, the breadth of the claims, and the lack of direction provided by the Applicants, it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 6-8, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benfey *et al.* (U.S. Patent Application Publication 2002/0173017), in view of Iwamura *et al.* (1983, *J. Medicinal Chem.* 26(6): 838-844). The instant claims are drawn to methods of transforming cells with cytokinin receptors and screening for agonists by measuring changes in these cells. Benfey *et al.* teach WOL, which is nearly identical to one of the cytokinin receptors identified by Applicants as SEQ ID NO: 6 (also, see Rashotte *et al.* (2003), *Plant Physiology*, 132: 1998-2011 which teaches that the WOL gene is the same as CRE1, a cytokinin histidine kinase receptor). Thus, the protein as taught by Benfey *et al.* is within the scope of the claims. Benfey *et al.* teach plant cells transformed with recombinant constructs expressing the WOL gene (paragraph 0137). Furthermore, Benfey *et al.* teach identification of ligands to the WOL cytokinin receptor (paragraph 0151). Benfey *et al.* also teach that WOL is a two-component signal transducer. Moreover, Benfey *et al.* teach methods for identifying compounds that modulate the activity of a WOL polypeptide comprising contacting the polypeptide with a test compound and determining the effect of the test compound on the activity of the polypeptide (see claims 6 and 17 and paragraph 0121). Benfey *et al.* further teach that the WOL gene products may be expressed in yeast (page 12, paragraph 133), such as the budding yeast *Saccharomyces*. However, Benfey *et al.* do not teach a method for analyzing agonist activity wherein intracellular signal transduction is measured.

Iwamura *et al.* teach a method of exposing cells expressing cytokinin receptors to cytokinin receptor agonists and antagonists. Iwamura *et al.* further teach measuring cytokinin receptor activity by measuring the fresh weight yield of a tobacco callus, *i.e.* measuring cell propagation (p. 839). Applicants state on p. 28 that "the existence or the quantity of intracellular signal transduction means, for example, the quantity of the cell growth of the transformed cell as an indicator." Thus, it would have been prima facie obvious to a person of ordinary skill in the art to modify the method as taught by Benfey *et al.* by measuring changes in signal transduction

as taught by Iwamura *et al.* Motivation to do so is provided by Iwamura *et al.* in that they teach measuring the effects of agonists on cytokinin receptors, and the WOL gene as taught by Benfey *et al.* is a cytokinin receptor. One of ordinary skill in the art would have expected the modified method to work as well as the one exemplified.

Conclusion

NO CLAIMS ARE ALLOWED.

The following prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

WO 02/099079 A2 Sheen *et al.*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (703) 305-0634. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm. Please note for your records that as of approximately January 20, 2004, the examiner's new telephone number will be (571) 272-0886.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RBK
12/22/03

JANET ANDRES
PATENT EXAMINER